FILE 'CAPLUS' ENTERED AT 15:19:10 ON 03 MAR 2006

=> S BETA AMYLOID;S SERUM ALBUMIN
       1366276 BETA
          1325 BETAS
       1366349 BETA
                  (BETA OR BETAS)
         23039 AMYLOID
          1674 AMYLOIDS
         23127 AMYLOID
                  (AMYLOID OR AMYLOIDS)
L1   7381 BETA AMYLOID
                  (BETA(W)AMYLOID)

        543476 SERUM
         16749 SERUMS
         45898 SERA
             9 SERAS
        567713 SERUM
                  (SERUM OR SERUMS OR SERA OR SERAS)
        123923 ALBUMIN
         81579 ALBUMINS
        144606 ALBUMIN
                  (ALBUMIN OR ALBUMINS)
L2   57032 SERUM ALBUMIN
                  (SERUM(W)ALBUMIN)

=> S L1(5A)L2
L3   1 L1(5A)L2

=> D CBIB ABS

L3   ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
2005:49386 Document No. 143:95024 Immunochemical crossreactivity of antibodies specific for "advanced glycation endproducts" with "advanced lipoxidation endproducts". Richter, Torsten; Munch, Gerald; Lueth, Hans-Joachim; Arendt, Thomas; Kientsch-Engel, Rosemarie; Stahl, Peter; Fengler, Doerte; Kuhla, Bjoern (Neuroimmunological Cell Biology Unit, Interdisciplinary Center of Clinical Research (IZKF), Leipzig, Germany). Neurobiology of Aging, 26(4), 465-474 (English) 2005. CODEN: NEAGDO. ISSN: 0197-4580. Publisher: Elsevier B.V..

AB Antibodies against advanced glycation endproducts (AGEs) are used for their immunohistol. localization in tissues, for example in Alzheimer's disease (AD) or diabetes. Many monoclonal and polyclonal antibodies have been used, and their specificity is unknown in most cases. Increased radical production, leading to the formation of lipid-derived reactive carbonyl species, such as malondialdehyde (MDA), acrolein, and glyoxal, is a characteristic aspect of age-related diseases like Alzheimer's disease or diabetic polyneuropathy. These reactive carbonyl species are able to modify proteins, resulting in AGE related structures, termed "advanced lipoxidn. products" (ALEs). In this study, the monoclonal carboxymethyllysine-specific antibody 4G9 and the polyclonal AGE-antibody K2189 were tested for their immunoreactivity towards these carbonyl-derived protein modifications. To investigate which carbonyl-modified amino acid side chains are specifically recognized by these antibodies, peptide membranes were incubated with glyoxal, MDA and acrolein. As model proteins, microtubuli associated protein tau (MAP-tau), . **beta.-amyloid**, human **serum albumin** and chicken egg albumin were incubated likewise. It was found that both antibodies detected reaction products of these carbonyl compds. on lysine- and arginine residues and for the protein modification, it was found that some epitopes might not be detected. In conclusion, AGE-antibodies might not only detect sugar-derived AGEs but also structures derived from lipid peroxidn. products (serving as markers of oxidative stress).

=> S L1(L)L2
L4 11 L1(L)L2

=> S L4 NOT L3
L5 10 L4 NOT L3

=> D 1-10 CBIB ABS

L5 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2004:946506 Document No. 142:21558 Transferrin neutralization of amyloid β 25-35 cytotoxicity. Giunta, Sergio; Galeazzi, Roberta; Valli, M. Beatrice; Corder, Elizabeth H.; Galeazzi, Luciano (Laboratorio Analisi Chimico-Cliniche, Microbiologiche e Diagnostica Molecolare, Ospedale Geriatrico INRCA (IRCCS), Ancona, 60100, Italy). Clinica Chimica Acta, 350(1-2), 129-136 (English) 2004. CODEN: CCATAR. ISSN: 0009-8981. Publisher: Elsevier B.V..

AB Fibrillar aggregates of amyloid β 25-35 (Aβ25-35) form rapidly in vitro able to lyse human red blood cells (RBCs). Human **sera**, **albumin**, and apolipoprotein E (ApoE) each limit fibrillation and cytotoxicity. Potentially, these substances protect neurons from Aβ1-40/42 aggregates. Transferrin (TF) is investigated in this study. The Mattson red blood cells model was employed to determine whether co-incubation of transferrin and Aβ25-35 prevented lysis. The formation of fibrillar Aβ25-35 in the presence of transferrin was investigated using Congo red staining and spectrophotometric studies. The authors found that incubation of 20 μM Aβ25-35 with physiol. levels of transferrin prevented red blood cells lysis and the formation of macro-aggregates. These in vitro results suggest that transferrin may limit fibrillar β **amyloid** formation in vivo and cytotoxicity.

L5 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1999:666471 Document No. 132:345048 99mTc-MAMA-chrysamine G, a probe for beta-amyloid protein of Alzheimer's disease. Dezutter, Nancy A.; Dom, Rene J.; de Groot, Tjibbe J.; Bormans, Guy M.; Verbruggen, Alfons M. (Laboratory of Radiopharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, K. U. Leuven, Louvain, Belg.). European Journal of Nuclear Medicine, 26(11), 1392-1399 (English) 1999. CODEN: EJNMD9. ISSN: 0340-6997. Publisher: Springer-Verlag.

AB Chrysamine G (CG), an analog of Congo red, is known to bind in vitro to the β-**amyloid** protein (Aβ 10-43) and to homogenates of several regions of the brain of Alzheimer's disease (AD) patients. We synthesized a conjugate of 2-(acetamido)-CG with a bis-S-trityl protected monoamide-monoaminedithiol (MAMA-Tr2) tetraligand, which was efficiently deprotected and labeled with a 75% yield with technetium-99m, to obtain 99mTc-MAMA-CG. In mice, 99mTc-MAMA-CG was cleared mainly by the hepatobiliary system, resulting in a fast blood clearance. Brain uptake of 99mTc-MAMA-CG was low. Co-injection with the blood pool tracer iodine-125 human **serum albumin** (125I-HSA) demonstrated a brain/blood activity ratio for 99mTc-MAMA-CG that was significantly higher than that for 125I-HSA (t test for dependent samples, $P<0.02$), indicating the ability of 99mTc-MAMA-CG to cross the blood-brain barrier. In vitro autoradiog. demonstrated pronounced binding of 99mTc-MAMA-CG to β-**amyloid** deposits in autopsy sections of the parietal and occipital cortex of an AD patient as compared with controls. Adding 10 mM Congo red during incubation displaced the binding of 99mTc-MAMA-CG. Congo red staining and autoradiog. identified the same lesions. 99mTc-MAMA-CG seems to bind selectively to . **beta.-amyloid** deposition in human brain parenchyma and blood vessels in vitro and thus might be a lead compound for further development of a useful tracer agent for the in vivo diagnosis of Alzheimer's disease.

L5 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1997:92914 Document No. 126:210517 Apolipoprotein E4 (ApoE4) but not ApoE3

or ApoE2 potentiates β-amyloid protein activation of complement in vitro. McGeer, Patrick L.; Walker, Douglas G.; Pitas, Robert E.; Mahley, Robert W.; McGeer, Edith G. (Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, Can.). Brain Research, 749(1), 135-138 (English) 1997. CODEN: BRREAP. ISSN: 0006-8993. Publisher: Elsevier.

AB Apolipoprotein E4 (ApoE4) increases the risk of late-onset Alzheimer's disease (AD). It binds tightly to **β-amyloid** protein (Aβ), which is known to activate the classical complement pathway in vitro. Since complement activation is a possible mechanism for promoting inflammation in AD, the authors tested, utilizing ELISA techniques, whether the various isoforms of ApoE could influence Aβ complement activation, or could themselves activate the pathway. Aβ applied alone to ELISA plate wells at concns. of 100-500 ng showed a linear increase in ability to activate serum complement, but all the ApoE isoproteins were inactive. When 200 or 430 ng of Aβ were plated and then exposed to solns. of 100-200 ng of ApoE2, ApoE3, ApoE4 or bovine **serum albumin** (BSA), only ApoE4 significantly enhanced the activation. This ApoE4-specific enhancement of complement activation by Aβ may relate to its role in increasing the risk of late-onset AD.

L5 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1996:331099 Document No. 125:55297 Apolipoprotein E is highly susceptible to oxidation by myeloperoxidase, an enzyme present in the brain. Jolivalt, C.; Leininger-Muller, B.; Drozdz, R.; Naskalski, J. W.; Siest, G. (URA CNRS 597, Centre du medicament, 30 rue Lionnois, Nancy, 54000, Fr.). Neuroscience Letters, 210(1), 61-64 (English) 1996. CODEN: NELED5. ISSN: 0304-3940. Publisher: Elsevier.

AB Apolipoprotein E, the most common apolipoprotein found in the brain, is linked to several pathologies like Alzheimer's disease. Apolipoprotein E directly binds to **β-amyloid** with a strong affinity. Myeloperoxidase, a protein secreted by neutrophils and involved in the inflammatory process, is also present in the brain. In vitro myeloperoxidase oxidation of recombinant human apolipoprotein E leads to fragmentation of the protein with low concns. of hydrogen peroxide and polymerization with higher concns. Comparison with bovine **serum albumin** shows a higher susceptibility of apolipoprotein E to myeloperoxidase oxidation, which may have importance in the Alzheimer's disease process.

L5 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1996:286905 Document No. 125:7353 Neurocytopathic effects of β-amyloid-stimulated monocytes: A potential mechanism for central nervous system damage in Alzheimer disease. London, Jill A.; Biegel, Diane; Pachter, Joel S. (Dep. Physiol., Univ. Connecticut Health Cent., Farmington, CT, 06030, USA). Proceedings of the National Academy of Sciences of the United States of America, 93(9), 4147-4152 (English) 1996. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Growing evidence indicates that cells of the mononuclear phagocyte lineage, which includes peripheral blood monocytes (PBM) and tissue macrophages, participate in a variety of neurodestructive events and may play a pivotal role in neurodegenerative conditions such as Alzheimer disease. The present study sought to determine whether exposure of PBM to . **beta.-amyloid** peptide (Aβ), the major protein of the amyloid fibrils that accumulate in the brain in Alzheimer disease, could induce cytopathic activity in these cells upon their subsequent incubation with neural tissue. PBM were incubated with Aβ for 3 days, centrifuged and washed to remove traces of cell-free Aβ, and then applied to organotypic cultures of rat brain for varying periods of time. By using a cell-viability assay to quantitate neurocytopathic effect, an increase in the ratio of dead to live cells was detected in cultures containing Aβ-stimulated PBM vs. control PBM (stimulated with either bovine **serum albumin** or reverse Aβ peptide) as early as 3 days after coculture. The ratio of dead to live cells increased further by 10 days of coculture. By 30 days of coculture, the dead to live cell ratio remained

elevated, and the intensity of neurocytopathic effect was such that large areas of brain mass dissociated from the cultures. These results indicate that stimulation of PBM with Aβ significantly heightens their neurocytopathic activity and highlight the possibility that inflammatory reactions in the brain play a role in the neurodegeneration that accompanies Alzheimer disease.

L5 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1996:162488 Document No. 124:229038 The fibril forming region of the β-amyloid precursor differs from that of the amyloid A precursor in its interaction with lipids. Liang, J. S.; Fine, R. E.; Abraham, C. R.; Sipe, J. D. (Dep. Biochemistry, Boston Univ. School Medicine, Boston, MA, 02118, USA). Biochemical and Biophysical Research Communications, 219(3), 962-67 (English) 1996. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Academic.

AB Since the amyloid A (AA) precursor, serum amyloid A (apoSAA), has been shown to bind cholesterol (C) in the AA fibril forming region, the authors investigated the interaction of the **β-amyloid** precursor protein (AβPP) and **β-amyloid** (Aβ) peptide with C and phosphatidylcholine (PC) by measuring changes in binding to microtiter wells at physiol. pH and ionic strength. While either C or PC inhibited AβPP binding to the same extent that C inhibited apoSAA binding, neither C nor PC had any effect on binding of the Aβ peptide, although antibodies to Aβ1-40 did block binding. The binding of 125I-Aβ1-40 and 125I-AβPP was inhibited by apoE3 and apoE4, but not by either apoSAA or bovine **serum albumin.** Bound 125I-AβPP was partially released into medium containing C, PC, apoE3, apoE4, or antibodies to AβPP. Thus, AβPP but not Aβ peptide can be retained in solution in the presence of C and PC and this failure to interact with lipids may account for the greater insoly. of Aβ fibrils than AA fibrils.

L5 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1995:654232 Document No. 123:77510 Differential binding of vascular cell-derived proteoglycans (perlecan, biglycan, decorin, and versican) to the beta-amyloid protein of Alzheimer's disease. Snow, Alan D.; Kinsella, Michael G.; Parks, Esther; Sekiguchi, Raymond T.; Miller, John D.; Kimata, Koji; Wight, Thomas N. (Dep. Pathology, Univ. Washington, Seattle, WA, 98195-6480, USA). Archives of Biochemistry and Biophysics, 320(1), 84-95 (English) 1995. CODEN: ABBIA4. ISSN: 0003-9861. Publisher: Academic.

AB Previous studies have demonstrated the immunolocalization of perlecan, a specific heparan sulfate proteoglycan, to the **beta- amyloid** protein (Aβ)-containing amyloid deposits within the walls of blood vessels (i.e., congophilic angiopathy) in Alzheimer's disease (AD) brain. In the present investigation, the differential binding of previously characterized endothelial cell (EC)- and smooth muscle cell (SMC)-derived PGs to Aβ was examined to determine whether the accumulation of Aβ in cerebrovascular amyloid deposits may be due to its interactions with perlecan. Pretreatment of AA amyloidotic splenic and liver tissue sections with synthetic Aβ (1-28) produced strong immunoreactivity with Aβ antibodies at tissue sites enriched in perlecan which was partially removed by pretreatment with heparitinase, but not by chondroitin ABC lyase. [35S]-Sulfate labeled proteoglycans (PGs) derived from cultured ECs and SMCs bound to affinity columns containing Aβ (1-28) or (1-40),with virtually no binding to Aβ (40-1) (reverse peptide), **beta-amyloid** precursor protein (410-429), or bovine **serum albumin.** Characterization of EC and SMC PGs bound to Aβ (1-28) revealed strong binding by perlecan, weak binding by decorin and biglycan, two dermatan sulfate proteoglycans, and lack of binding by versican/PG-M, a large chondroitin sulfate proteoglycan. Binding of 125I-labeled perlecan to Aβ (1-28) was strongly inhibited by isolated perlecan and to a lesser extent by heparin, but not by chondroitin-6-sulfate or unsulfated dextran sulfate. Heparitinase treatment decreased, but did not eliminate the binding of 125I-labeled perlecan to Aβ (1-28)- and EC-derived perlecan in solid-phase assays indicated high-affinity (Kd =

8.3+10-11 M) and lower-affinity (Kd = 4.2+10-8 M) binding sites, with approx. 1 mol of perlecan binding 1.8 mol of Aβ. A significant decrease in binding of EC-derived perlecan to Aβ (1-28) was observed when a sequence within the putative heparin-binding motif of Aβ (His13His14Gln15Lys16) was replaced by the uncharged peptide sequence, Gly13Gly14Gln15Gly16, indicating a perlecan binding site on Aβ near the postulated alpha-secretase site (at Lys-16). Overall, the results indicate that specific vascular cell-derived PGs differentially interact with Aβ, and that the interactions of highest affinity occur between Aβ and binding sites on both the core protein and glycosaminoglycan chains of perlecan. The selective affinity of vascular cell-derived perlecan for Aβ may account for the accumulation of Aβ in conjunction with perlecan in cerebrovascular amyloid deposits in AD brain.

L5 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1995:556729 Document No. 122:312242 Ca2+-dependent binding of human serum amyloid P component to Alzheimer's β-amyloid peptide. Hamazaki, Hideaki (Dep. Biology, Kitasato Univ., Kanagawa, 228, Japan). Journal of Biological Chemistry, 270(18), 10392-4 (English) 1995. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Serum amyloid P component (SAP), a normal glycoprotein, is universally found in amyloid deposits, including cerebrovascular amyloid of Alzheimer's disease. This paper describes the Ca2+-dependent binding of human SAP to Alzheimer's **β-amyloid** peptide (Aβ). 125I-SAP binds to synthetic human Aβ-(1-40) immobilized on microtiter plates at a dissociation constant of 6.0+10-9M in 0.01M Tris-HCl, 0.15M NaCl, pH 7.5, containing 2 mM Ca2+, 1% bovine **serum albumin**, and 0.05% Tween 20. Binding inhibition assay has shown that soluble Aβ-(1-40) and Aβ-(1-28) also bind to SAP. Since SAP is resistant to proteases in the presence of calcium, the Ca2+-dependent binding of SAP to soluble Aβ and to **β-amyloid** fibrils would give pathol. effects on fibril formation and persistence of **β-amyloid** in Alzheimer's disease.

L5 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1994:531568 Document No. 121:131568 Apolipoprotein E associates with β amyloid peptide of Alzheimer's disease to form novel monofibrils. Sanan, David A.; Weisgraber, Karl H.; Russell, Stephen J.; Mahley, Robert W.; Huang, David; Saunders, Ann; Schmechel, Donald; Wisniewski, Thomas; Frangione, Blas (Gladstone Inst. Cardiovascular Disease, Univ. California, San Francisco, CA, 94141-9100, USA). Journal of Clinical Investigation, 94(2), 860-9 (English) 1994. CODEN: JCINAO. ISSN: 0021-9738.

AB Late-onset and sporadic Alzheimer's disease are associated with the apolipoprotein E (apoE) type 4 allele expressing the protein isoform apoE4. Apolipoprotein E binds avidly to **β amyloid** (Aβ) peptide, a major component of senile plaque of Alzheimer's disease, in an isoform-specific manner. The apoE4 isoform binds to Aβ peptide more rapidly than apoE3. The authors observed that soluble SDS-stable complexes of apoE3 or apoE4, formed by co-incubation with Aβ peptide, precipitated after several days of incubation at 37° with apoE4 complexes precipitating more rapidly than apoE3 complexes. Aβ(1-28) and Aβ(1-40) peptides were incubated in the presence or absence of apoE3, apoE4, or bovine **serum albumin** for 4 d at 37° (pH 7.3). Neg. stain electron microscopy revealed that the Aβ peptide alone self-assembled into twisted ribbons containing two or three strands but occasionally into multistranded sheets. The apoE/Aβ co-incubates yielded monofibrils 7 nm in diameter ApoE4/Aβ co-incubates yielded a denser matrix of monofibrils than apoE3/Aβ co-incubates. Unlike purely monofibrillar apoE4/Aβ co-incubates, apoE3/Aβ co-incubates also contained double- and triple-stranded structures. Both apoE isoforms were shown by immunogold labeling to be uniformly distributed along the Aβ peptide monofibrils.

Monofibrils appeared earlier in apoE4/Aβ than in apoE3/Aβ in time-course expts. Thus apoE3 and apoE4 each interact with β **amyloid** peptide to form novel monofibrillar structures, apoE4 more avidly, a finding consistent with the biochem. and genetic association between apoE4 and Alzheimer's disease.

L5 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1993:122248 Document No. 118:122248 A novel protein in calf serum recognizes β-amyloid in the formalin-fixed section. Kanemaru, Kazutomi; Hasegawa, Masato; Ihara, Yasuo (Dep. Neurophysiol., Tokyo Metrop. Inst. Gerontol., Tokyo, Japan). International Congress Series, 999(β-Amyloid Precursor Proteins Neurotransm. Funct.), 61-71 (English) 1991. CODEN: EXMDA4. ISSN: 0531-5131.

AB A proteinaceous component (CSX) in the calf serum, presumably a minor fraction of bovine **serum albumin**, is considered to recognize only distinct forms of β-pleated sheets, regardless of their constituents. Using CSX as a probe, we conclude that 1) meningovascular β-**amyloid** should have a β-pleated sheet structure somewhat dissimilar to that of . **beta.-amyloid** cores; (2) most of β-protein immunoreactivities in the diffuse plaque in AD or normal aged brains should reflect small amts. of amyloid fibrils in the normal-appearing neuropil.

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=> S AMYLOID
         23039 AMYLOID
          1674 AMYLOIDS
L6       23127 AMYLOID
                (AMYLOID OR AMYLOIDS)

=> S L6(6A)L2
L7          17 L6(6A)L2

=> S L7 NOT L4
L8          15 L7 NOT L4

=> D 1-15 CBIB ABS
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L8 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2006:32289 Document No. 144:127500 Dual specific scFv antibodies antagonizing human TNF-α and serum protein for treating rheumatoid arthritis and other inflammatory disorders. Ignatovich, Olga; De Wildt, Rudolf; Woolven, Benjamin; Grant, Steven; Jones, Philip; Basran, Amrik; Brewis, Neil (Domantis Limited, UK). PCT Int. Appl. WO 2006003388 A2 20060112, 540 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-GB2553 20050629. PRIORITY: GB 2004-2829 20040630; US 2004-2004/925366 20040824; US 2005-2005/98758 20050404.

AB The invention relates to compns. and methods for treating inflammatory disorders. More specifically, the invention relates to antibody compns. and their use in the treatment of inflammatory disorders. The antibodies are dual specific single domain antibodies specific to human TNF-α and an antigen other than TNF-α such as VEGF or serum protein including fibrin, α2-macroglobulin, **serum albumin** , fibrinogen A, fibrinogen, serum **amyloid** protein A, heptaglobin, ubiquitin, uteroglobulin and β2-microglobulin. The treatment may further comprises administration of at least one addnl. therapeutic agent selected from

corticosteroids, NSAIDs, acetylsalicylic acid, pyrazolones, fenamate, diflunisal, etc.

L8 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2005:681668 Document No. 143:281991 Protein sample concentration by repeated loading onto SDS-PAGE. Sheen, Hyukho; Ali-Khan, Zafer (Department of Microbiology and Immunology, McGill University, Montreal, QC, H3A 2B4, Can.). Analytical Biochemistry, 343(2), 338-340 (English) 2005. CODEN: ANBCA2. ISSN: 0003-2697. Publisher: Elsevier.
AB The concentration of dilute protein solns. for subsequent SDS-PAGE was investigated using 1- to 3-cm-long stacking gel of discontinuous SDS-PAGE. Up to 5 times repeated loading of mixts. containing bovine **serum albumin** and glutathione S-transferase/serum **amyloid** A1 fusion protein showed a single protein band. There was no effect on protein band resolution in the presence of 137 mM NaCl and with 4 times loading.

L8 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2005:170779 Document No. 143:324032 Serum albumin: a late-reacting negative acute-phase protein in clinically evident inflammation in dialysis patients. Tsirpanlis, George; Bagos, Pantelis; Ioannou, Dimitris; Bleta, Aliki; Marinou, Ioanna; Lagouranis, Antonis; Chatzipanagiotou, Stylianos; Nicolaou, Chrysoula (Department of Nephrology, University of Athens, Greece). Nephrology, Dialysis, Transplantation, 20(3), 658-660 (English) 2005. CODEN: NDTREA. ISSN: 0931-0509. Publisher: Oxford University Press.
AB C-reactive protein (CRP), serum amyloid A (SAA), interleukin-6 and S-albumin were measured for 16 consecutive weeks in 37 hemodialysis (HD) patients and every inflammatory clin. event during this time period was recorded. CRP and SAA were found to be neg. but insignificantly correlated with S-albumin measured immediately (1-7 days) after a clin. event. However, anal. of the same correlation with S-albumin measured in the following week (7-14 days from a clin. event) showed that this became highly significant for CRP and SAA, and changed for IL-6. In addition, in weeks with clin. events, CRP in the group of HD patients included in the study was indicative of a 'real inflammation' while in the weeks free of clin. events this pos. acute-phase protein was significantly lower, indicating a microinflammatory process. These findings may explain the unexpected result in the study of Nascimento et al. (2004) showing that S-albumin in HD patients behaves as a neg. acute-phase protein but with a delay of 1-2 wk after a clin. significant inflammation.

L8 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2004:364079 Document No. 141:388368 Statin therapy improves cardiovascular outcome of patients with peripheral artery disease. Schillinger, Martin; Exner, Markus; Mlekusch, Wolfgang; Amighi, Jasmin; Sabeti, Schila; Muellner, Marcus; Rumpold, Helmut; Wagner, Oswald; Minar, Erich (Department of Internal Medicine II, Division of Angiology, Medical School, Vienna General Hospital, Vienna, A-1090, Austria). European Heart Journal, 25(9), 742-748 (English) 2004. CODEN: EHJODF. ISSN: 0195-668X. Publisher: Elsevier Science B.V..
AB Aims: We sought to examine the interrelationship between statin use, inflammation, and outcome of high-risk patients with advanced atherosclerosis. Methods and results: We prospectively studied 515 patients with severe peripheral artery disease (median age 70 yr, 296 males). The cardiovascular risk profile and laboratory parameters of inflammation (high-sensitivity C-reactive protein [hs-CRP], serum **amyloid** A [SAA], fibrinogen, **serum albumin**, neutrophil counts) were obtained, and patients were followed for a median of 21 mo (interquartile range 12-25) for the occurrence of myocardial infarction (MI) and death. We observed 19 MIs (5 fatal and 14 nonfatal) and 65 deaths. Cumulative survival and event-free survival rates (freedom from death and MI) at 6, 12, and 24 mo were 97%, 95%, and 89%, and 96%, 93% and 87%, resp. Patients receiving statin therapy

(n=269, 52%) had a lower level of inflammation (hs-CRP p<0.001, SAA p=0.001, fibrinogen p=0.007, albumin p<0.001, neutrophils p=0.049) and better survival (adjusted hazard ratio [HR] 0.52, p=0.022) and event-free survival rates (adjusted HR 0.48, p=0.004) than patients not treated with statins. However, patients with low inflammatory activity (hs-CRP ≤0.42 mg/dL) had no significant benefit from statin therapy (p=0.74 for survival; p=0.83 for event-free survival), whereas in patients with high hs-CRP (>0.42 mg/dL) statin therapy was associated with a significantly reduced risk for mortality (adjusted HR 0.58, p=0.046) and the composite of myocardial infarction and death (adjusted HR 0.46, p=0.016). Conclusion: Statin therapy is associated with a substantially improved intermediate-term survival of patients with severe peripheral artery disease and a high inflammatory activity, whereas in patients with low hs-CRP no survival benefit was observed

L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

2004:298899 Document No. 140:389809 All-trans retinoic acid is increased in the acute phase-related hyporetinemia during Escherichia coli mastitis. Van Merris, V.; Meyer, E.; Duchateau, L.; Blum, J.; Burvenich, C. (Department of Physiology, Biochemistry and Biometrics, Faculty of Veterinary Medicine, Ghent University, Merelbeke, B-9820, Belg.). Journal of Dairy Science, 87(4), 980-987 (English) 2004. CODEN: JDSCAE. ISSN: 0022-0302. Publisher: American Dairy Science Association.

AB Blood vitamin A profiles, including concns. of retinol and its active metabolite retinoic acid, were assessed during the peripartum period and during exptl. induced Escherichia coli mastitis in heifers. Serum retinol decreased in all animals in the immediate postpartum period and normalized within 1 wk after parturition. No significant changes were detectable in the concns. of retinoic acid isomers during puerperium. Following intramammary E. coli infusion, all cows showed moderate symptoms of systemic disease besides the local signs of inflammation. The presence of a systemic acute-phase reaction was documented by fever, increase in serum **amyloid** A, and decrease in **serum albumin.** Retinol concentration in serum also decreased spectacularly during coliform mastitis, and the decline was clearly related to the timing of the acute-phase response. Moreover, a significant increase of all-trans retinoic acid, mirrored by a lowering of 13-cis retinoic acid, was detected during the same time period. The 9-cis isomer of retinoic acid was present in all samples, but it remained below the quantification limit. Results confirmed the decrease in serum retinol during the peripartum period of dairy cows. Furthermore, the study established that profound changes in vitamin A metabolism occur during the acute-phase reaction of coliform mastitis in heifers. The bovine infection model reproduced the acute phase-related hyporetinemia, as previously observed in humans and rats. In addition, all-trans retinoic acid was found to be the most abundant circulating acid isomer during mastitis, providing an indication for a possible key role of all-trans retinoic acid in the modulation of the immune response.

L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

2004:209516 Document No. 140:319271 Serum albumin predicts cardiac adverse events in patients with advanced atherosclerosis - interrelation with traditional cardiovascular risk factors. Schillinger, Martin; Exner, Markus; Mlekusch, Wolfgang; Amighi, Jasmin; Sabeti, Schila; Schlager, Oliver; Wagner, Oswald; Minar, Erich (Departments of Angiology, Medical School, Vienna General Hospital, Vienna, A-1090, Austria). Thrombosis and Haemostasis, 91(3), 610-618 (English) 2004. CODEN: THHADQ. ISSN: 0340-6245. Publisher: Schattauer GmbH.

AB Low serum albumin is a powerful predictor of cardiovascular adverse events in healthy subjects and patients with subclin. atherosclerosis. We investigated the association between serum albumin, traditional cardiovascular risk factors, markers of inflammation and cardiovascular outcome in 515 patients with advanced atherosclerosis and severe peripheral artery disease. Cardiovascular risk profile, **serum albumin**, serum **amyloid** A (SAA) and fibrinogen were obtained at baseline, and patients were followed for median 21 mo (interquartile range 12 to

25) for the occurrence of major adverse cardiac events (MACE: myocardial infarction, percutaneous coronary interventions, coronary artery bypass graft, and death). We observed 135 MACE in 109 patients (21%). Cumulative event-free survival rates at 6, 12, and 24 mo were 95%, 91%, and 80%, resp. Low albumin predicted MACE independently of SAA and fibrinogen. Adjusted hazard ratios for the occurrence of MACE, any death, and the composite of death and MI according to increasing quartiles of albumin were 2.40, 1.14 and 1.09 ($p<0.001$), 2.94, 1.34 and 1.11 ($p=0.003$) and 3.63, 1.86 and 1.29 ($p<0.001$), resp., as compared to the highest quartile. Considering albumin in conjunction with traditional cardiovascular risk factors (smoking, hyperlipidemia, hypertension and diabetes), we found that low albumin predicted MACE only in patients with a low risk profile (less than 3 risk factors) ($p<0.001$), whereas low albumin was not associated with MACE in patients with three or more risk factors ($p=0.66$). We conclude that low serum albumin is associated with cardiovascular outcome of patients with advanced atherosclerosis adding to the prognostic information of other inflammatory markers, and may be particularly useful for risk prediction in patients with few traditional risk factors.

L8 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

2003:822529 Document No. 139:392657 Glycation Induces Formation of Amyloid Cross-β Structure in Albumin. Bouma, Barend; Kroon-Batenburg, Loes M. J.; Wu, Ya-Ping; Bruenjes, Bettina; Posthuma, George; Kranenburg, Onno; De Groot, Philip G.; Voest, Emile E.; Gebbink, Martijn F. B. G. (Department of Medical Oncology, University Medical Center Utrecht, Utrecht, 3584 CX, Neth.). Journal of Biological Chemistry, 278(43), 41810-41819 (English) 2003. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Amyloid fibrils are components of proteinaceous plaques that are associated with conformational diseases such as Alzheimer's disease, transmissible spongiform encephalopathies, and familial amyloidosis. Amyloid polypeptides share a specific quaternary structure element known as cross-β structure. Commonly, fibrillar aggregates are modified by advanced glycation end products (AGE). In addition, AGE formation itself induces protein aggregation. Both amyloid proteins and protein-AGE adducts bind multiligand receptors, such as receptor for AGE, CD36, and scavenger receptors A and B type I, and the serine protease tissue-type plasminogen activator (tPA). Based on these observations, we hypothesized that glycation induces refolding of globular proteins, accompanied by the formation of cross-β structure. Using TEM, we demonstrate here that glycated albumin condensates into fibrous or amorphous aggregates. These aggregates bind to amyloid-specific dyes Congo red and thioflavin T and to tPA. In contrast to globular albumin, glycated albumin contains amino acid residues in β-sheet conformation, as measured with CD spectropolarimetry. Moreover, it displays cross-β structure, as determined with x-ray fiber diffraction. We conclude that glycation induces refolding of initially globular albumin into amyloid fibrils comprising cross-β structure. This would explain how glycated ligands and amyloid ligands can bind to the same multiligand "cross-β structure" receptors and to tPA.

L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1994:505101 Document No. 121:105101 The interaction of human serum albumin in the native and fully reduced states with apolipoprotein E, serum amyloid protein and very low density lipoproteins from human plasma. Dergunov, Alexander D.; Vorotnikova, Yliya Y. (Natl. Res. Cent. Preventive Med., Moscow, 101953, Russia). International Journal of Biochemistry, 26(7), 933-42 (English) 1994. CODEN: IJBOBV. ISSN: 0020-711X.

AB Complex formation in a solution of apolipoprotein E (apoE) isolated from human plasma very-low-d. lipoproteins (VLDL) and human serum albumin (HSA) in both native and fully reduced states was studied. The existence of a kinetically unstable complex of apoE and native albumin was shown. The complex became more stable with the reduction of the S-S links in the albumin mols. capable of

forming aggregates under these conditions. The interaction between native HSA as opposed to a fully reduced one and isolated VLDL particles was more pronounced, probably due to the existence of amphipathic alpha-helical regions. Dissociation of the serum amyloid protein (SAP) oligomeric form in solution and the interaction of the protein with fully reduced HSA owing to the provision with the addnl. hydrophobic surface was shown. ApoE displaced SAP from the complex with fully reduced albumin. It is suggested that the ability of the apolipoprotein to interact with albumin is determined by internal stability of the mol. structure of the latter and the complexes detected in vitro may be a new transport form of apolipoproteins in lipid-free form in serum. It is assumed that competitive interactions in the HSA-SAP-apoE system may be involved in the development of secondary amyloidosis.

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1993:664350 Document No. 119:264350 Comparative toxicity of amyloid β-peptide in neuroblastoma cell lines: Effects of albumin and physalaemin. Zhao, Xiaohong; Valantas, Julie A.; Vyas, Sandip; Duffy, Lawrence K. (Inst. Arctic Biol., Univ. Alaska, Fairbanks, AK, 99775-0180, USA). Comparative Biochemistry and Physiology, Part C: Pharmacology, Toxicology & Endocrinology, 106C(1), 165-70 (English) 1993. CODEN: CBPCEE. ISSN: 0742-8413.

AB Synthetic amyloid β-peptide was toxic to NB41A3 neuroblastoma cells in serum-free culture as judged by decreasing cell nos. and release of the cytosolic enzyme, lactic dehydrogenase. Without **amyloid** β-peptide, bovine **serum albumin** increased the number of cells surviving in culture. In the presence of amyloid β-peptide, BSA appeared to potentiate the amyloid β-peptide toxicity. The toxic dose response for amyloid β-peptide varied between different cell lines (NB41A3, NB2a and IMR32), in a range of 100-1000 nM amyloid β-peptide. Amyloid β-peptide toxicity was inhibited by the concurrent treatment of the cells with the tachykinin physalemin with an ED50 of 10-6M.

L8 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1984:549339 Document No. 101:149339 'Amyloid degrading activity' of human serum, an in vitro clearing effect which does not involve degradation of amyloid fibrils. Caspi, D.; Baltz, Marilyn L.; Feinstein, A.; Munn, E. A.; Pepys, M. B. (Dep. Med., R. Postgrad. Med. Sch., London, W12 0HS, UK). Clinical and Experimental Immunology, 57(3), 647-56 (English) 1984. CODEN: CEXIAL. ISSN: 0009-9104.

AB Clearing of turbid amyloid A fibril containing agarose gels by human serum has been ascribed to 'amyloid degrading activity'. It is reported here that this optical phenomenon is not due to an enzymic reaction, does not involve proteolysis of the fibril subunits and is not inhibited by sera of patients with AA amyloidosis. The extent of clearing correlates closely with the serum albumin concentration and, as previously reported by others, serum albumin itself causes clearing comparable to that of whole serum. Furthermore addition of albumin solns. to turbid aqueous suspensions of AA amyloid fibrils causes immediate clearing. **Serum albumin** is known to clarify turbid non-**amyloid** fibril containing gels and is used com. to improve the optical properties of radial immunodiffusion plates. It is proposed that this property of albumin, the mechanism of which is not yet understood, underlies the so called 'amyloid degrading activity' of human serum.

L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1979:414894 Document No. 91:14894 Some effects of the administration of endotoxin in mice. Specific cleavage of serum albumin by an acid protease and the generation of amyloid serum component. Gorevic, Peter D.; Levo, Yoram; Chatpar, Prem C.; Frangione, Blas; Franklin, E. C. (Med. Cent., New York Univ., New York, NY, 10016, USA). Journal of Clinical Investigation, 63(2), 254-61 (English) 1979. CODEN: JCINAO. ISSN: 0021-9738.

AB Endotoxin induced amyloidosis in mice and resulted in the appearance in serum of large amts. of amyloid-related protein (SAA). After injection of 300 μg lipopolysaccharide from Escherichia coli into mice SAA behaved as an acute phase reactant with levels reaching a peak of >600 μg/mL at 18-22 h and returning to base line (<50 μg/mL) by 48 h in each of 4 strains tested; only the endotoxin-resistant C3H/HeJ strain showed a smaller response. Lesser elevations were also found after s.c. injection of 25 mg of casein, bovine serum albumin, ovalbumin, or monomeric Ig G, whereas pyrogen-free human serum albumin failed to raise SAA levels. SAA generation may thus be a result of endotoxin contamination of these protein prepns. Also present in equivalent amts. in acidified serum from endotoxin-treated mice, but barely detectable in control sera, was a 3000-dalton mol. whose amino acid sequence was identical to the amino terminal 24 residues of mouse albumin. The appearance of SAA and the amino terminal albumin fragment after endotoxin were unaffected by pretreatment with cobra venom factor. Pretreatment with pepstatin in vivo, or before acidification in vitro, prevented the appearance of the albumin fragment but had no effect on the appearance of SAA, whereas leupeptin and antipain did not affect the appearance of either SAA or the albumin fragment. Probably, the generation of SAA after endotoxin administration does not involve complement activation or intravascular proteolytic activity, whereas the liberation of a specific peptic-like cleavage product of albumin may be the consequence of an acid protease.

L8 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1977:532097 Document No. 87:132097 Serum amyloid A (SAA) protein - interaction with itself and serum albumin. Rosenthal, C. Julian; Franklin, Edward C. (Dep. Med., Downstate Med. Cent., Brooklyn, NY, USA). Journal of Immunology, 119(2), 630-4 (English) 1977. CODEN: JOIMA3. ISSN: 0022-1767.

AB Serum amyloid A (SAA) protein is a 12,000 dalton protein that exists in serum under physiologic conditions as an 85,000 dalton complex and under certain conditions, as a 170,000 dalton component. To study the reason for this finding, the behavior of 125I-labeled SAA was studied in the presence of cold SAA and several serum proteins. SAA caused a shift of some of the radioactivity to the region of albumin. Addition of normal human serum or albumin caused a shift of a significant fraction of the radioactivity to a peak eluting slightly ahead of albumin (80,000 daltons). This interaction could be blocked by the addition of cold SAA. No shift was noted when IgG or Bence Jones proteins were added. Thus, it appears that low mol. SAA protein has a tendency to aggregate with itself and to bind to albumin but not to human IgG or Bence Jones proteins.

L8 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1977:153409 Document No. 86:153409 Kinetics of serum amyloid protein A in casein-induced murine amyloidosis. Benson, Merrill D.; Scheinberg, Morton A.; Shirahama, Tsuranobu; Cathcart, Edgar S.; Skinner, Martha (Evans Dep. Clin. Res., Univ. Hosp., Boston, MA, USA). Journal of Clinical Investigation, 59(3), 412-17 (English) 1977. CODEN: JCINAO. ISSN: 0021-9738.

AB The murine model of casein-induced amyloidosis was studied to determine the relation between blood serum amyloid protein A (SAA) production and amyloid deposition. SAA levels were as high as 200 times the normal level in CBA/J mice receiving daily parenteral casein. After a single injection of casein the SAA level was elevated by 3 h and peaked by 12-18 h. Similar levels were found in casein-treated A/J mice, a strain less susceptible to the induction of amyloid. Parenterally administered bovine **serum albumin**, which has low potential for **amyloid** induction, gave SAA levels in CBA/J and A/J mice comparable to casein treatment. Thus, while SAA levels are elevated during chronic antigenic stimulation, there are other factors involved in amyloid formation. These factors may include alterations in the degradation of SAA by the reticuloendothelial system caused by substances such as casein. Nude (athymic) mice attained high levels of SAA after receiving casein parenterally. Therefore, thymus-derived lymphocytes are not necessary for synthesis of SAA.

L8 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1966:87059 Document No. 64:87059 Original Reference No. 64:16418a-c Serum protein and glycoprotein patterns in spontaneous mouse amyloidosis. Gray, G. R.; Pearce, R. H.; Taylor, H. E. (Univ. British Columbia, Vancouver, Can.). Archives of Pathology, 81(2), 129-35 (English) 1966. CODEN: ARPAAQ. ISSN: 0363-0153.

AB Serum protein analyses were performed on blood from 54 mice of a strain (SM/ML) which developed amyloidosis with age and from 43 mice of a nonamyloid strain (C57BL). In both strains there was a gradual increase in protein-bound hexose with age, but no significant difference between the 2 strains. Electrophoresis revealed that there was an increase in the β-globulin fraction in animals showing moderate to marked amyloidosis, but not in those animals showing little amyloid. Both strains of mice showed a gradual increase in serum total protein with age up to 9 months, and thereafter there was a decrease in the nonamyloid strain. In the **amyloid** strain **serum albumin** remained fairly constant, whereas in the nonamyloid strain there was a decrease in serum albumin after 9 months of age. An increase in the serum α2-globulin fraction appeared to be associated with the progression of amyloidosis and an increase in serum β-globulins had a pos. correlation with the severity of the disease. There were no differences in serum γ-globulins between the 2 strains. The increases in serum α2- and β-globulins in older mice with amyloid was not apparent in the preamyloid or early amyloid phases, and may have been a nonspecific serum protein pattern reflecting generalized tissue damage. 35 references.

L8 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

1957:63389 Document No. 51:63389 Original Reference No. 51:11546g-i Disappearance of iodinated human-serum albumin in amyloidosis. Perasalo, O.; Tala, P.; Kyllonen, K. E. J.; Lieto, J. V. (Wihuri Research Inst., Helsinki). Ann. Med. Internae Fenniae, 45, 145-50 (English) 1956.

AB The rate of disappearance of iodinated human-**serum albumin** (IHSA) in nephrotic patients with **amyloid**, and in cases of nephrosis in which no amyloidosis could be revealed by the Congo red test, was studied. No difference was found in the 2 groups. However, these patients showed a higher rate of IHSA disappearance than patients with no albuminuria. An increased plasma volume was also found in these patients.

	L #	Hits	Search Text	DBs
1	L1	3323	BETA ADJ AMYLOID	US-PGPUB; USPAT
2	L2	66368	SERUM ALBUMIN	US-PGPUB; USPAT
3	L3	144	L1 SAME L2	US-PGPUB; USPAT